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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,914	06/22/2001	Claire Dubois	85761-28	5893

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EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/885,914	DUBOIS, CLAIRE	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) *32-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed, 11-30-05, is acknowledge. Claims 21-40 were added and claims 1-20 were canceled. Claims 21-40 are pending in this application.

2. Newly submitted claims 32-40 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The newly submitted claims are drawn to a method of inhibiting synovial cell growth in a mammal comprising administering an effective amount of proprotein convertase inhibitor. This method is independent and distinct from the treatment of inflammation or erosive aspect of arthritis because this method can be used to treat other diseases. For example, synovial cell have been implicated in distinct disease, from arthritis and inflammation, such as psoriasis, hyperkeratosis and hyperplasia. Thus, the method of treating arthritis and inflammation may utilize different patient populations and different end-points.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 32-40 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. In their election, dated 12-27-04, Applicants elected as the species, "any compound capable of inhibiting a proprotein convertase." A search was conducted on this species and was found in the prior art, alpha-antitrypsin-portland. Those claims that read on this species have been rejected. Those claims that do not, such as 23 and 26, have been withdrawn from consideration. See MPEP 803.02.

4. All rejection made in the previous office action and not cited herein are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 21-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the previous office action, under the rejection of 35 USC 112 rejecting claims 1-18, and the reasons set forth below.

Applicants argue that support for a "proprotein converatse" may be found on page 9 of the specification where it states "'. . .[f]urin like protease activity includes activity proprotein convertases such as PACE4, PC5/6 or PC7." Further derivatives of PDX may be found in US 6022855 and on page 5 of the specification. Example 6 at pages 23-26 discloses the administration of PDC, Dec-RVKR-CH2Cl. Thus, the instant specification provide amble written guidance.

Applicants arguments have been fully considered but have not been found persuasive.

Reviewing US No. 6022855, the US patent does not teach nor disclose proprotein convertase inhibitors. The only context the word derivative appears is in the context of a furin analog lacking the carboxy terminal 81 amino acids. This however is not defined to be a proproetin converatase inhibitor. While the instant specification defines of PDC and Dec-RVKR-CH2Cl, it does not provide any written description for any PDX derivative. Applicants have not provide

sufficient evidence that derivatives of PDX were well known in the art and hence they were in possession of the entire scope of the claim.

Rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 21-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas et al. (US 6022855) or Jean, et al. (WO 99/516624) in view of Blanchette et al. and Allen et al.

The claims are drawn to method of treating inflammatory or erosive aspects of arthritis in a mammal comprising administering a therapeutically effective amount of proprotein convertase inhibitor.

Thomas and Jean et al. were discussed in the previous office action and those discussion, including discussion regarding administration, are incorporated into this rejection.

Thomas and Jean both teach that the antitrypsin Portland molecule is a potent furin inhibitor. For example, Thomas et al. shows, in figure 2, the inhibition of furin by antitrypsin Portland. The Thomas reference further states that the methods of the invention encompass inhibition of proteolytic processing of any biologically active molecule that is proteolytically processed by furin in vivo or in vitro, including but not limited to peptide hormones, neuropeptides, growth factors, coagulation factors, serum albumin, cell surface receptors, and adhesion molecules.

Preferred biologically active proteins are pro-.beta.-nerve growth factor, blood coagulation factor protein Factor IX, pro-von Willibrand factor, complement factor C3 and renin, for alleviation of pathological conditions and disease states in an animal, preferably a human, associated with over-expression, over-production or otherwise inappropriate synthesis of such biologically-active proteins (see col. 8, lines 36-60). The difference between the prior at and the instant application is that the references combined do not teach the treatment of inflammatory or erosive aspects or arthritis.

However, Blancehtte et al. teaches TGFβ is processed by furin. Furin is responsible for the proteolytic maturation of TGFβ-1 (see page 1977) and can elevate concentration of biologically available mature TGFβ-1 (see page 1981). .

Allen et al. teach that TGFβ-1 was found to induce synovial erythema, swelling, and leukocyte infiltration (see page 231, abstract). The reference further states that TGFβ is a key mediator of the events associated with SCW-induced arthritis (see page 244). The reference states that the data suggest that TGFβ, released by platelets and activated inflammatory cells, may play a direct role in leukocyte recruitment and activation in arthritic and other chronic inflammatory lesions (see page 245). Therefore it would have been obvious to treat inflammatory or erosive aspects of arthritis with the antitrypsin Portland of Thomas/Jean et al. One would have been motivated to do so because antitrypsin Portland is a furin inhibitor. Since TGFβ is processed by Furin and is responsible maturation of TGFβ-1, one would expect that inhibition of furin would result in decrease of TGFβ-1 which would in-turn result in the benefiting the inflammatory aspects of arthritis. This is because data suggest that TGFβ, released by platelets and activated inflammatory cells, may play a direct role in leukocyte recruitment and activation in arthritic and other chronic inflammatory lesions.

For these reasons, the reference combined render obvious the claimed invention.

Response to Applicants Arguments

The rejection has been altered with the addition of the new reference of Allen et al. However, to expidite prosecution some of Applicants argument, to the extent they are pertinent to the rejection, have been addressed.

Applicants argue that the prior art relied upon is not pertinent to the particular problem with which the inventor was concerned and is not analogous art. None of the reference, independently or when combined, teach all of the elements/steps of the claimed method of treating the inflammatory and/or erosive aspects of arthritis. Thomas et al. is directed to viral/bacterial infections which are completely unrelated to Applicants claimed invention. Further, the Wang reference and Yaminishi references are not prior art with respect to the claimed invention.

First, the rejection no longer relies upon or mentions Wang and Yamnishi references. Thus, those arguments are moot. With respect to Thomas/Jean et al. it is respectfully submitted that the references are analogous and pertinent to the claimed invention. Thomas/Jean teach the antitrypsin Portland molecule claimed in the instant application. Further, the references teach that the antitrypsin is capable of inhibition of proteolytic processing of any biologically active molecule that is proteolytically processed by furin in vivo or in vitro, including but not limited to peptide hormones, neuropeptides, growth factors, coagulation factors, serum albumin, cell surface receptors, and adhesion molecules. It is the secondary references of Blanchette et al. and Allen et al. that provide the nexus between the furin inhibitory activity and the treatment of arthritis.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach

the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.

8/4/10

Anish Gupta
Patent Examiner